Tyson (J.)

DOES THE PRESENT STATE OF KNOWLEDGE JUSTIFY A CLINICAL AND PATHOLOGICAL CORRELATION OF RHEUMATISM, GOUT, DIABETES, AND CHRONIC BRIGHT'S DISEASE?

BY

JAMES TYSON, M.D., *Referee*,

PHILADELPHIA.

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As it is the object of the discussion proposed to arrive at a conclusion as to whether the diseases named are in any way or degree the result of the same pathological process, and therefore reciprocal or interchangeable, it may be well to state briefly, at the outset, what appear to me to be the prevailing views as to what constitutes each of them.

First, as to rheumatism, by which presumably is meant articular rheumatism: it is a general disease associated with an acute or a subacute inflammation of the articular and periarticular tissues, preferably of the larger joints, in a person possessed of a tendency thereto, which may be hereditary or acquired. No *materies morbi*, which can be held responsible for the disease, has ever been isolated, although upon theoretical grounds there is reason to believe that some such substance is present in the blood. The products of the inflammation are in no way peculiar or specific.

Gout is also a general affection accompanied by arthritis, preferably of the smaller joints, to the production of which a tendency, also hereditary or acquired, is necessary. That an undue accumulation of uric acid in the blood is responsible for the symptomatology is conceded by most to have been established by Garrod as far back as 1848. The arthritis is more or less constantly associated with deposits of sodium urate in the joints and their vicinity.

Diabetes mellitus is a disease more difficult to define in a few words, but clinical experience has established the existence of at least two varieties quite different in their pathology, which may be named the

milder and more severe forms. In both there is deranged function of the liver, as the result of which its cells are incapable of dehydrating glucose into glycogen, but permit it to pass as glucose through the portal vessels, and thence into the general circulation.

The method in which this one result is brought about in the two forms is, however, widely different. In the milder, it is probably the result of a habitual ingestion of a large amount of saccharine and amylaceous food, and consequent overstimulation of the glycogenic function, which, by exhausting either the liver cells or the secretory nerves in connection with them, interferes with their metabolic power. Thus the general circulation becomes surcharged with glucose. Accompanying this paralyzed state of the liver cells, and perhaps contributing to it, there is probably an exaggeration of the physiological hyperæmia which is always present in the liver during digestion. Under this form come many cases of glycosuria easily curable by dietetic regulation.

In the more severe form of diabetes, which may be termed the neurotic or neurogenous form, the dilatation of the hepatic bloodvessels and accelerated movement of the blood are due to a lesion in some more distant part, very frequently in the cerebro-spinal or sympathetic nervous system, which affects directly or by reflexion the vasomotor centre. Thus again, as in the well-known puncture of Bernard, and other experimental lesions of the cerebro-spinal and sympathetic nervous systems, an intermediate hyperæmia and accelerated circulation of the liver are produced, as a result of which the glucose is carried through that organ too rapidly to permit its proper metabolism. To the glucose contributed primarily by the intestinal digestion of starchy and saccharine foods only, is added in the more advanced stages that derived from the imperfect metabolism of albuminous foods. These include the stubborn cases of diabetes relieved, but not cured, by dietetic treatment, in many of which too, notwithstanding the evident involvement, primarily or secondarily, of the nervous system, the most carefully conducted autopsies often fail to discover any lesion.

If there be intended in the question such form of chronic Bright's disease as clinical experience has shown to be sufficiently often associated with any of the other three affections to justify the suspicion that there is some relation between them, we must include both inter-

stitial and parenchymatous nephritis, since the former occurs in connection with gout, and the latter with diabetes. No definition of either is required.

In looking about for facts, either clinical or pathological, which go to show a common process in these affections, it will be necessary to range alongside the morbid phenomena which are common to two or more of them, as well as those which differ, and to estimate them at their true value. Thus we note that both rheumatism and gout are arthritic affections, and an essential part of the morbid anatomy of both is an inflammation of the joints, and although the same class of joints is not always involved, this fact does not exclude a common etiological factor. We need not, therefore, dwell on this difference. Continuing our study of the morbid anatomy in rheumatism, we find changes in the synovial membranes and to a less degree in the cartilages, ligaments, and tendinous sheaths, which, as already stated, are in no way peculiar or specific, but such as we expect to result from simple inflammation. In gout, on the other hand, the articular exudates are loaded with urates, chiefly of sodium, but they are also said to include those of lime, magnesium, and ammonium. The watery portion of the exudate is absorbed and leaves the salts deposited in acicular crystalline forms on the synovial surfaces, in the cartilage cells and intercellular substance, in the tendons, ligaments, and bursæ, and in the subcutaneous connective tissue.

There are other changes about the joints in gout, but they are not specific. Such are the hyperplastic processes in the adjacent fibrous and connective tissues, resulting in more or less deformity. On the other hand, the arterial sclerosis and subsequent fatty and limy infiltration of the thickened bloodvessel coats may be regarded as specific, although not peculiar.

The blood changes to which we naturally look for that which constitutes essentially the two diseases, are widely different. Ignoring changes which have no direct bearing on the question, in rheumatism there is no excess of either uric acid or lactic acid. It is true that Latham has recently asserted[1] that uric acid resulting from the excessive formation of glycocine in muscular tissue is the *materies morbi* of

[1] Croonian Lectures on "Some Points in the Pathology of Rheumatism, Gout, and Diabetes," British Medical Journal, April, 1886, p. 676.

acute rheumatism, but the assertion is founded on purely theoretical grounds. In gout, on the other hand, the presence in the blood of uric acid in excess—in combination with sodium—is generally acknowledged and has been abundantly demonstrated. It is true that it is not invariably demonstrable, and true also that uric acid has been found in the blood of healthy individuals, but the invariable tendency to the deposit of its compounds in the joints, a deposit which can only come from the blood, proves an inseparable association of this substance with the disease.

While heredity is admitted by most observers to operate in the production of both diseases, it is far more conspicuous in gout than in rheumatism, ranging in different observations from 50 to almost 100 per cent., while the highest proportion claimed for rheumatism is but 34.6 per cent. Again, while it cannot be denied that gout, in cases of strong hereditary predisposition, may present itself even before puberty, yet the majority of patients are past forty when the first attack is developed; while rheumatism is a disease of early life, all statistics showing the largest percentage between fifteen and thirty-five years. Alcoholic liquors have no influence in the causation of true articular rheumatism, while in the production of gout they are all-powerful. Overindulgence in food has never been regarded as a factor in the causation of rheumatism, while insufficiency of food is a potent cause. The reverse is true of gout.

The extreme rarity of kidney disease in rheumatism, as contrasted with its almost invariable presence in gout, implies an important difference in the *materies morbi*, since the renal complication in the latter disease is admittedly due to the operation of an irritant circulating with the blood. Were the same or a like irritant present in the blood in rheumatism, we would expect a similar complication.

A gouty endocarditis is said to be not uncommon, yet it needs no lengthy argument to show that there is nothing comparable in gout to the cardiac complications of rheumatism. On the other hand, the skin diseases and catarrhal affections so characteristic of gout are unknown in rheumatism.

Whether rheumatism be engrafted upon a tendency slowly or rapidly acquired, through hereditation or otherwise, the exciting cause is always cold or dampness, or both. Not so with gout. The cause of the explosion or acute attack as manifested in the local

inflammation is the cause of the disease itself—the irritant substance in the blood—whether it be uric acid or some allied excrementitious substance, and whatever increases this or diminishes the power of resistance of the organism to its presence, produces the acute attack. Such causes are most frequently errors in diet, errors involving quality as well as quantity; the use of certain alcoholic drinks, whether moderate or excessive, the effect of all of which is to cause an accumulation of the noxious substance, either by directly increasing its formation or diminishing its excretion. Although atmospheric influences, such as sudden reduction of temperature or of atmospheric pressure, and even injuries, such as blows and contusions, are cited as being exciting causes of local attacks, they may be regarded either as the spark which ignites the inflammable material, or as operating to diminish the power of resistance of the organism to the action of the poison.

Considerable stress has been laid upon the argument from therapeutics to show a correlation between rheumatism and gout, more particularly in the case of a single remedy—salicylic acid. That it is the remedy par excellence for rheumatism no one who has had any experience with it will deny. That it is also very useful in gout there can be no doubt. Further, its action in gout is explainable on thoroughly rational and scientific grounds. It is now regarded as established that at least the chief seat of urea formation is the liver. This is accomplished by the metabolic action of its cells on the amido bodies—glycocine, taurine, leucin, and tyrosin—which result from the splitting up of bile and albuminoid substances during intestinal digestion. These are absorbed and carried directly to the liver, where they are converted chiefly into urea and carbonic acid. Whatever interferes with this conversion results in an accumulation of uric acid in the blood.[1]

Since the transforming power resides in the cells, it is plain that they may be overstimulated by an excess of these nitrogenous matters introduced into the portal blood, and that their normal office may be deranged. They would then cease to convert all the glycocine into urea, and the blood would become surcharged with uric acid. Now, if a substance could be introduced into the blood which would seize

[1] The chemical steps of this process as laid down by Latham in the Croonian Lectures referred to, are exceedingly interesting, but would be out of place here.

upon glycocine or its antecedent, methene cyan-alcohol, it would take away that which is essential to the formation of uric acid, and prevent accumulation of the latter in the blood. Such a substance is salicylic acid, and this is the way in which it probably acts. Practice and theory in this matter are further confirmed by experiment, since Salkowski and Noel Paton have both shown that salicylic acid increases the elimination of urea, while it diminishes that of uric acid. It is by reasoning backward from this point, along with the fact that salicylic acid is useful in rheumatism, it appears to me, that Professor Latham has come to the conclusion that uric acid is also the *materies morbi* of rheumatism. A moment's reflection, however, shows the insufficiency of such reasoning to prove the presence, in one disease, of a substance not recognizable by tests in such disease, while its presence in another is so easy of demonstration. Similar reasoning may also make lactic acid the morbid material of rheumatism; for the same antecedent of glycocine, by condensation of two of its molecules forms lactic and carbonic acids, and by seizing on such antecedent, salicylic acid also interferes with the formation of lactic acid. But, unfortunately, there is no more ground for considering lactic acid the *materies morbi* of acute rheumatism, than there is for assigning to uric acid the same *rôle*. Even the highly acid perspiration fails to yield lactic acid, and it has even been suggested by Bernier that the acidity is a post-secretion process, chiefly the result of chemical changes in the overheated and macerated surface of the skin and its epidermis.

Failing to discover any constituent of the blood which it is the saving office of salicylic acid to destroy, we are compelled to characterize the action of the acid by the unsatisfactory word "specific;" in doing which, however, we are no worse off than we are in explaining the action of quinine in intermittent fever and iodide of potassium in syphilis. Or may it not act like colchicum in gout, which, according to Lauder Brunton, paralyzes the sensory nerves, while the motor nerves and muscles are unaffected, and by so doing counteract the irritating effect of the poison, whatever it may be, while nature is gradually eliminating it? With regard to colchicum in rheumatism, if it is useful, it is probably by acting as it does in gout, as an anæsthetic.

Except in the case of salicylic acid, the remedies for gout are not the remedies for rheumatism. There is reason to believe that remedies which act upon the liver are among the best for gout and for clearing

up the cloudy urine which accompanies it. Such are the mercurials, blue mass and calomel, in purgative doses: such are magnesian and sodic sulphates, and especially the natural mineral waters in which these predominate—Carlsbad, Hunjadi, Marienbad, Friedrichshalle, and Pullna. Such are salicylate of sodium and benzoate of sodium, the influence of both of which in increasing the amount of urea and diminishing that of uric acid has been experimentally shown by Salkowski and Noel Paton.

Not so is it with rheumatism, which is not relieved, but is rather aggravated by the class of cathartics named, and which requires the blood to be built up, rather than depleted. The correct treatment for rheumatism cannot be regarded as eliminative; that for gout is eminently so. Such facts as these lead me to believe that the agency which produces rheumatism is something distinct and different from that which produces gout. The pathological processes, although somewhat similar, are not identical: while the clinical differences, including complications and sequelæ, are still more marked. Further, a chemical study of the blood discovers in gout a constituent which, wherever found, is acknowledged to possess the properties of an irritant, while no such substance is found in the blood of rheumatism. Finally, the therapeutics of the two diseases furnishes but an imaginary support to the view that the diseases are interchangeable.

The association of gout with that form of chronic renal disease known as contracted kidney, has long been a matter of observation with the physician and pathologist. To the fact that the man who has been the victim of gout, for any length of time, has also a contracted kidney, there are, indeed, few exceptions. And here there is abundant reason to believe they are the result of the same cause—that the relation is a true correlation, that whatever is the cause of gout is one of the causes of chronic interstitial nephritis: for, as is well known, the latter disease has many causes. That uric acid is one of these, is abundantly attested. That it is an irritant to the kidney, I think is evident from the fact that, with careful testing, almost never do we find abundant and continuous sediments of uric acid and urates, unaccompanied by a small albuminuria; while, if the uratic sediment is cleared up, and if it has not been of too long standing, albuminuria is cleared away simultaneously.

Such a correlation as is claimed for these two diseases is illustrated and confirmed by a case like the following: The mother of a girl of twelve recently consulted me because her daughter, although seemingly well, complained of a constant weariness, and the nurse had noted that the child's urine was always turbid, regardless of the temperature of the room in which it was kept. I found the urine loaded with uric acid and urates. That passed on rising had a specific gravity of 1.036, and was free from albumin: that passed in the evening had a specific gravity of 1.037; contained about one-twenty-fifth its bulk of albumin, considerable mucus, some so-called mucous casts, and a few epithelial cells. On inquiry, I found the child's father an almost constant sufferer from gout, and so were his father and grandfather before him. Such an albuminuria may truly be called a gouty albuminuria. In this case a few grains of citrate of potash, freely diluted and given three times a day, a vegetable diet, and the free use of milk, promptly reduced the specific gravity, and caused the disappearance of the albumin. The practical importance of the knowledge of such a tendency cannot be overestimated.

Much more difficult is it to determine the precise relation between gout and diabetes. Let us begin by comparing and contrasting symptoms, and especially study those which have been regarded as common to both. In both affections there is a urine of high specific gravity, but in gout the specific gravity is due to the larger proportion of uric acid salts associated with a diminished rather than an increased proportion of water, while in diabetes the specific gravity and quantity of water increase *pari passu*, the increased weight of the urine being due to glucose. As gout progresses, and the kidneys become secondarily involved, the specific gravity of the urine declines, while, with unarrested diabetes the weight of the urine keeps on increasing.

While sediments of uric acid and urates are constant in the urine of gout, the more than usual occurrence of a sediment of uric *acid* in diabetes has long been a matter of observation. Notwithstanding this, all exact quantitative examinations I have been able to consult, including those of Haughton,[1] Seegen,[2] Riess and Naunyn,[3] go to show

[1] Phenomena of Diabetes Mellitus. Dublin Quart. Journ. Med. Sci., Oct. 1868.
[2] Der Diabetes Mellitus, Berlin, 1875, S. 91.
[3] Ueber den Diabetes, von Dr. Fr. Th. von Frerichs, 1884, S. 65.

that if the uric acid eliminated is not diminished in diabetes, it is certainly not increased. Whence it must be inferred that the sediments of uric acid found in diabetic urine are the result of the increased acidity which grows out of the fermentation processes so prone to be set up in saccharine urine. My own experience confirms that of Seegen and Pavy, that cases in which uric acid sediments appear are apt to be of the milder form, in which the quantity of urine is therefore not so great, but the proportion of urates is still sufficient to permit their decomposition by the acids of the fermented urine with precipitation of uric acid crystals.

It is also said that sugar is frequently found in the urine in cases of gout and lithæmia, but I am satisfied that this occurs less frequently than is commonly supposed, owing to the fact that uric acid reduces decidedly the salts of copper. I am sure this is not sufficiently appreciated by physicians. I know that in times past I have been myself misled by it again and again in the examination of lithæmic urines of high specific gravity, which differ from diabetic urines in being dark hued instead of light in color. Since I have become aware of this fact, I have never found sugar in these urines.

Another circumstance which may be said to favor a common origin for diabetes and gout is that which has been emphasized by my friend Dr. Draper, in his valuable article on gout, in the *System of Medicine* by American authors—the feeble capacity of gouty persons for the digestion of saccharine and amylaceous foods, and the fact that a diet similar to that which glycosuria requires, without the extreme restriction of the carbohydrates demanded by the latter, is the best for the gouty case. My experience in the treatment of gout has not been very large, but so far as it goes it coincides with that of Dr. Draper in this respect. I would, however, interpret the result somewhat differently. The indigestion and resulting acidity often noted to follow the ingestion of saccharine and amylaceous food, are due, in my view, to defective converting power in the digestive fluids of the stomach and intestines. In diabetes these fluids do not seem at fault. There is no failure to convert sugar and starch into glucose. The defect is in the liver itself, which fails to convert the glucose into glycogen, and allows it to pass into the general circulation.

But notwithstanding the fact that I believe some of the data on which is founded the idea of a correlation between gout and diabetes

have been erroneously interpreted, I still believe that between gout and the milder form of diabetes, or rather the non-neurogenous form—because I am not certain that all cases of neurogenous diabetes are severe—there is a certain correlation. This view is, perhaps, based upon physiological rather than clinical facts. As has been said, in both affections the liver is at fault. In one case the defect is in the metabolism of nitrogenous foods, resulting in the accumulation of uric acid in the blood; in the other it is in the metabolism of saccharine and amylaceous foods, resulting in the accumulation of glucose in the blood. This being the case, it is not unreasonable to expect the simultaneous occurrence of gout and diabetes in the same individual, or even the alternation of the two affections. I have never myself met such cases, but their occasional occurrence is recognized by clinicians. The general opinion of those who have met them is that they are more common in obese persons, and it is in these cases that the total withdrawal of the carbohydrates is said to be often undesirable, or even harmful. Such was the testimony of Hoffmann, of Dorpat, and of von Mehring, of Strasburg, during the discussion on diabetes at the recent Congress of German Physicians at Wiesbaden. The latter allows even bread, and says that patients are apt to retrograde on a pure meat diet, and to become the subjects of diabetic coma. He does not say why this is, but I should be disposed to regard such coma as uræmic, and a consequence of the almost inevitable contracted kidney, the presence of which would predispose to coma, especially in conjunction with a nitrogenous diet.

Very different are the relations of gout with the usually more severe or neurogenous form of diabetes. Here the primary cause is remote from the liver, and although the liver is secondarily hyperæmic, and the glycosuria is immediately due to the secondary hyperæmia, the essential cause is removed from the organ, while in all forms of gout it resides in it. Thus the glycosuria is the result of a disease more or less distant, while the lithæmic condition, although secondary to hepatic derangement, is the cause of the entire complexus of symptoms which constitute the clinical history of gout. Between this form of diabetes and gout there is, to my mind, no correlation whatever.

As to the relation of Bright's disease to diabetes, the occasional association of the two conditions has long been recognized, but it has

generally been thought that it is more particularly in the later stages of diabetes that albuminuria makes its appearance. Recently, however, in the discussion just alluded to, Stokvis, of Amsterdam, called attention to the fact that albuminuria is wanting in the minority of cases, even in the early stages. I regret very much that in a considerable experience with diabetes I have not until recently been in the habit of examining the urine for albumin early in the disease, but since I have commenced to do so the results have been such as to lead me to believe that Stokvis is correct. His experience is that the albuminuria is not constant. Now it coincides with the presence of sugar; again, it alternates with it. It may be present in quantities so small that it may be overlooked in the enormous dilution to which it is subjected by the polyuria. In other instances, again, it is the more conspicuous symptom. The albuminuria is ascribed to the irritative effect of the foreign substances—sugar, aceton, and diacetic acid—upon the epithelial cells of the kidney, while autopsies show that such albuminurias are generally associated with pathological changes in the kidney. Finally, intravenous injection of sugar is found to be attended with albuminuria so soon as the sugar in the urine reaches two per cent. The same effect follows the injection of aceton and diacetic acid.

It has always been conceded that the form of renal change associated with the more advanced forms of diabetes is parenchymatous nephritis, in which the epithelium is the primary point of attack. Now these observations go to show that the albuminurias of the early stages are attended by the same changes in slighter degree, and presumably brought about in the same way. This being the case, we find that both gout and diabetes are often accompanied by chronic Bright's disease, but by forms essentially different. Both are the result of noxious substances in the blood. In the instance of gout the noxious substance is at once the cause of the disease and the cause of the complication, while in the case of diabetes the noxious substance which is the cause of the complication is the result of the diabetes. So that it may be said there is a true correlation between gout and chronic Bright's disease in that the same cause may produce either condition. But in the case of diabetes the cause of the diabetes is not the cause of the chronic Bright's disease. It is rather the result of the diabetes which causes the renal complication.

Referring once more to therapeutics, the idea that rheumatism and diabetes are much more closely correlated than I have admitted them to be, has apparently received substantial support by the results of treatment of the latter disease by salicylic acid. The suggestion of salicylic acid as a remedy for diabetes is not a very recent one. I myself had occasion to allude to it as far back as 1881, but I am not aware that it has been regarded with favor until recently. My own experience with it, although limited, was not favorable. Recently, however, several practitioners in Philadelphia have told me that they have had satisfactory results from its use, and a new impulse to its use has arisen since the promulgation of Prof. Latham's views in the lectures alluded to. He concludes on chemical grounds that there are two forms of diabetes, one due to neurotic disturbance of the function of the liver, and the other to neurotic disturbance of the function of muscle, as the result of which glucose is produced in muscle, and passes thence into the circulation. This latter form he regards as closely related to rheumatism, so closely that one degree of oxidation develops the *materies morbi* of rheumatism—whatever that may be—and another develops glucose. Having also shown by the same reasoning that the administration of salicylic acid arrests the formation of uric acid, lactic acid, and glucose, he thus explains the usefulness of salicylic acid in some forms of diabetes, and says that given in doses of from ten to twenty grains three times a day he has seen it produce marked improvement. More recently Dr. J. Sinclair Holden reports, in *The British Medical Journal*,[1] six cases of diabetes complicated with rheumatic pains, treated with salicylic acid and a diet much less restricted than usually required, in all of which there was marked amelioration, and in three the sugar disappeared totally. In a fourth the sugar also disappeared, but on account of the indigestion produced by the medicine it could not be persevered in sufficiently to get rid of the sugar. Holden also tried the salicylic acid in four other cases in which no rheumatic symptoms existed, and in all failed to make any impression on the polyuria or sugar, although two improved on a restricted diet. All of these cases were under thirty, while the six cases of rheumatic nature were all over fifty.

These are indeed remarkable results, and I very much regret that I learned of them too late to make it possible to test them before pre-

[1] May 1, 1886.

paring this paper. Should they be substantiated, they would certainly go to establish a very much closer relation between rheumatism and diabetes than I have heretofore been willing to admit. From the clinical standpoint I can only say this, that in one of the cases which came under my observation in which salicylic acid was said to have been of great service, careful volumetric analysis showed that, so far from the sugar being diminished during the administration of the drug, it was positively increased. Such a result as this, taken in connection with the fact that the same efficiency has been claimed for a host of remedies which further use has shown to be utterly useless, produced in me an indifference which, in the light of these most recent results, I much regret.

Summary.

Rheumatism and gout are similar in that there is in each a *materies morbi* which is responsible for the symptoms of the disease. This *materies morbi* is, however, not the same in the two diseases, being in the case of gout uric acid, and in that of rheumatism undetermined. It is not impossible that in both instances the morbid material may produce its symptoms by operating upon or irritating some parts of the nervous system, as the spinal cord, and that the arthropathies and other symptoms are, therefore, in this sense neurotic. At the same time the symptomatic peculiarities of each disease, as well as its morbid anatomy, are the result of its own peculiar poison. The proof of this is found in the chemistry, the symptomatology, the morbid anatomy, the sequelæ and complications, and in the therapeutics of the two diseases.

Gout and diabetes can be compared only after subdividing the latter into its milder and more severe forms. The milder forms of diabetes and gout are similar, and in a sense correlated, in that in both the metabolic function of the liver cells is deranged. In the former the power to convert glucose into glycogen is lost, and in the latter is lost the power to convert glycocine and some other products of the breaking up of albuminoid substances into urea—resulting in the accumulation in the blood of urate of sodium. Both of these are the result of overstimulation of the liver cells by an excessive amount of food—in the case of gout, nitrogenous food, and in that of diabetes saccharine and amylaceous food.

Between gout and the more severe form of diabetes there is no correlation, this form being the result of morbid states in distant parts, influencing directly or indirectly the vasomotor centre, whence results a hyperæmia of the liver, with rapid movement of blood, and a too rapid transit of glucose through the liver to permit its conversion into glycogen. Observe that in this form of diabetes the glycosuria is the *result* of a primary neurosis, whereas if gout have a neurotic feature the uric acid is the cause of the neurotic disturbance by acting as an irritant upon the irritable nervous centres. Hence there is no correlation between gout and the second form of diabetes.

As to the correlation between diabetes and acute rheumatism, such can only exist in the event there is a third form of diabetes which might be termed muscular, in which neurotic disturbance is exerted upon muscle, in consequence of which there ensue incomplete oxidation of glycocolic acid, and the formation of glucose, which passes over into the circulation.

Based upon theory, and the results of treatment of a limited number of cases by salicylic acid, the question of the existence of such a form of diabetes cannot be regarded as ready for decision.

The relation of rheumatism, gout, and diabetes to chronic Bright's disease may be summed up as follows: that of rheumatism as purely accidental; that of gout and diabetes as causal. In the case of gout, the uric acid circulating in the blood acts as an irritant to the interstitial tissue of the kidney, causing its overgrowth and subsequent contraction; while in diabetes, the sugar and allied matters circulating in the blood act as irritants to the epithelium of the kidney, producing cloudy swelling or fatty change; in a word, slight degrees of parenchymatous inflammation, with or without corresponding enlargement of the entire organ.